Unraveling the Molecular Magic of Witchweed

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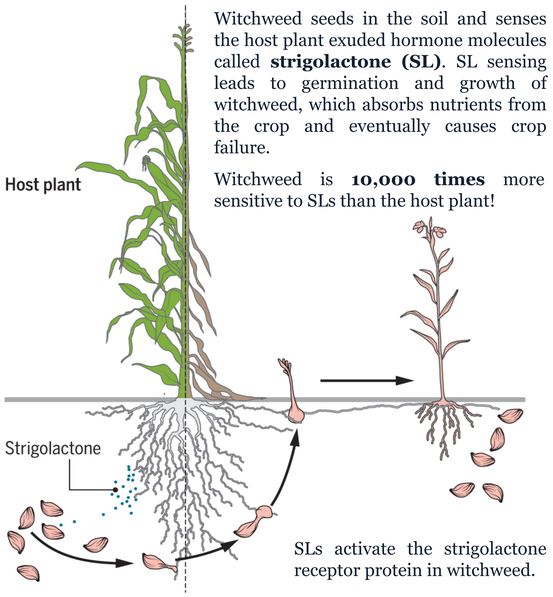
BACKGROUND

Witchweed is a root parasitic plant that causes damage to crops. Globally, it leads ***to economic loss of* $10 billion every year**, and loss to livelihood of over **100 million** farmers around the world**.**

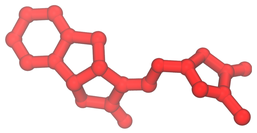


Witchweed seeds in the soil and senses the host plant exuded hormone molecules called **strigolactone (SL)**. SL sensing leads to germination and growth of witchweed, which absorbs nutrients from the crop and eventually causes crop failure.

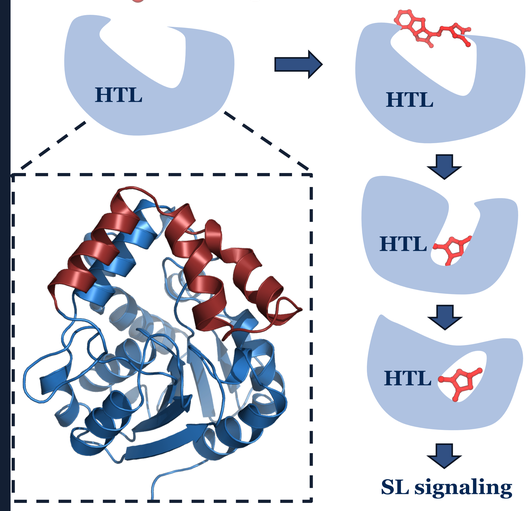
Witchweed is **10,000 times** more sensitive to SLs than the host plant!

SLs activate the strigolactone receptor protein in witchweed.

INTRODUCTION



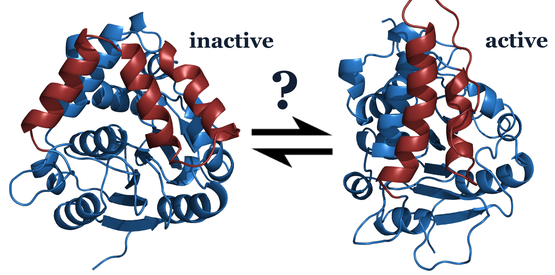
From a molecular perspective, SLs (red) are hydrolyzed by the receptor protein HTL (blue) and trigger the signaling process associated with the germination of parasite.



DRIVING QUESTIONS

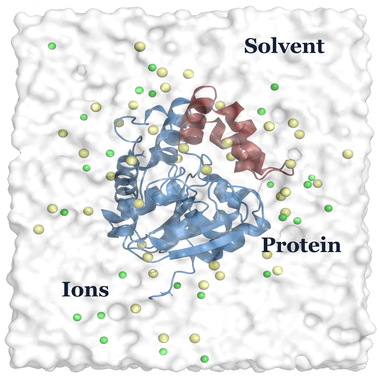
To develop a molecular control strategy that inhibits growth of witchweed to avoid crop failure, we need to understand activation process of the strigolactone receptors.

Here, we study the thermodynamics and kinetics of the activation mechanism and the effect of hydrolysis intermediate on the activation process.



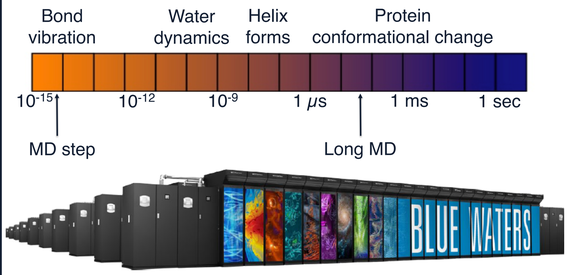
METHODS

Molecular Dynamics (MD) simulations mimic and predict the time evolution of a system of atoms, assuming a given potential energy function.



Forces are derived from the potential energy of the simulated system using the current atom positions:

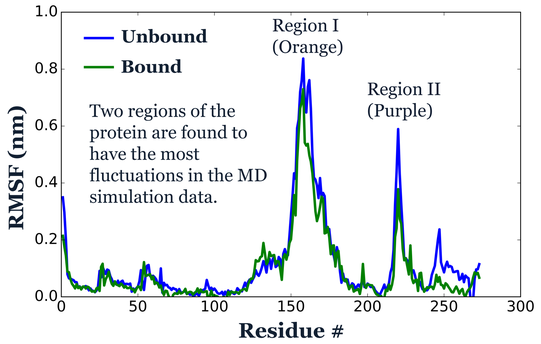
$$m\frac{d^2r_i}{dt^2} = F_i(r_1, r_2, \dots r_N) = \nabla_{r_i} U(r_1, r_2, \dots r_N) \quad (i = 1,2, \dots N)$$

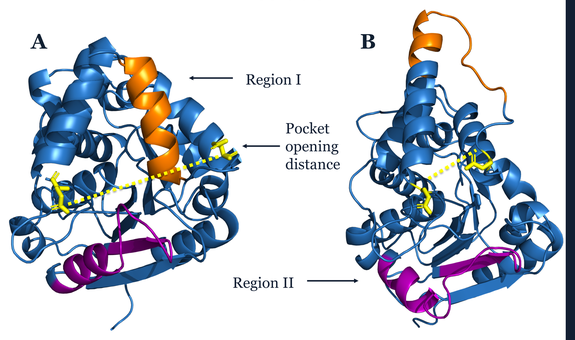


We collected ~70 μs of unbiased MD simulation data each **for both apo and intermediate bound** strigolactone receptors, using the **Blue Waters supercomputer**.

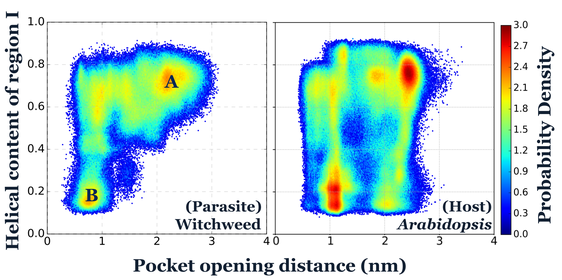
RESULTS

Root mean square fluctuations (RMSF) shows the deviations between the simulated structures and a reference structure of the protein.





Conformational landscapes of the simulation data projected on 2 metrics show differences in activation mechanism for apo and intermediate bound structures.



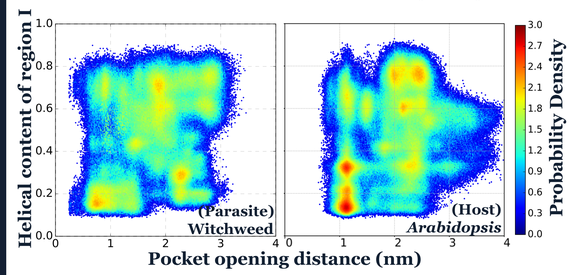
We compared our landscapes to a similar protein from *Arabidopsis* plant (host) which has a lower affinity to SLs.

Higher probability density regions are detected in the active and inactive states in host plant.

We can observe lower barrier of transition from inactive to active state in parasitic plant.

RESULTS

We observe alternative pathways between active and inactive states in parasite receptor **after hydrolysis**.

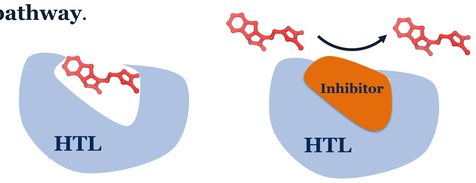


CONCLUSION

- Simulations reveal the flexible regions of the protein involved in the activation process.
- We determine that **intermediate-bound protein has more potential activation pathways** than the apo protein.
- We conclude that the witchweed protein has lower free energy for activation as compared to *Arabidopsis*. This might explain the higher SL affinity in witchweed germination.

FUTURE DIRECTIONS

- We will use **Markov State Models (MSMs)** to obtain conformational dynamics and thermodynamic properties of parasitic SL receptors upon ligand binding activation.
- With this study, we aim to understand the mechanism of SL hormone recognition of parasitic witchweed.
- Furthermore, by determining the intermediate states during activation, **we can identify the accessibility of the receptor pocket and provide insights to designing herbicides that inhibit the activation pathway**.



Signaling on

Signaling off, no witchweed growth

Publication:
Qihua Chen, Shriyaa Mittal, Zahra Shamsi, Diwakar Shukla, "Molecular Dynamics Simulation Reveals the Conformational Heterogeneity of the Strigolactone Receptor in Parasitic Plants", Manuscript in Preparation, 2018

References:
Pennisi, E. Science (2015); Toh, S. et al. Science (2015); Yao, R. et al. Nature (2016)

SHODOR

BLUE WATERS SUSTAINED PETASCALE COMPUTING

ILLINOIS